SUMMARY REPORT

on studies conducted through
U.S. EPA Region VIII
to evaluate the

SYSTEMIC AVAILABILITY OF LEAD TO YOUNG SWINE FROM SUBCHRONIC ADMINISTRATION OF LEAD-CONTAMINATED SOIL

(Phase II)

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April 3, 1996

for:

The Palmerton Citizens For A Clean Environment

In Response to Task Schedule #13, Item #2

OVERVIEW

The following report has been prepared in response to Task Schedule #13, Item #2, which requests a written review of the protocol for the pig study, titled: "Systemic Availability of Lead to Young Swine from Subchronic Administration of Lead-Contaminated Soil (Phase II)". Task Schedule #13, Item #2 also requests information regarding the suitability of young pigs as test subjects (the presumption is that suitable test subjects would have similar systemic availability - or bioavailability - characteristics to humans, specifically young children); and asks if the pig study accounts for (or adequately reflects) the multi-media exposure scenario that humans are subjected to in the Palmerton area.

To gain an understanding of the pig study, MKA Project Manager Robert H. Hosking Jr., reviewed the following documents:

1. The Project Manual and the Project Notebook (Revision 1) for *Systematic Availability of Lead to Young Swine from Subchronic Administration of Lead-Contaminated Soil (Phase II)*, which are similar documents, and were both prepared by Stan W. Casteel, V.M.D., Ph.D., Veterinary Medical Diagnostic Laboratory, University of Missouri-Columbia, Columbia Missouri (314) 882-6811.

Both were prepared for Roy F. Weston, Inc. 215 Union Boulevard, Suite 600, Lakewood, Colorado 80228 (303) 980-6800; For submission to: U.S. EPA Region VIII, Denver, Colorado. Document Control Numbers: 4800-30-0079 (Project Manual), and 4800-30-0127 (Project Notebook). The Project Manual included sections outlining the project Protocol; the Quality Assurance Project Plan; U.S. EPA Region VIII Bioavailability Study Standard Operating Procedures; and copies of 40 CFR Part 792 outlining Toxic Substances Control Act (TSCA) Good Laboratory Practice Standards, and 40 CFR Part 160 Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) Good Laboratory Practice Standards. The Project Notebook contains everything that is in the Project Manual, plus an expanded section outlining standard operating procedures and a section titled: Final Phase II Bioavailability Studies Sample Preparation and Analysis Report. The Sample Preparation and Analysis Report (EPA Work Assignment No. 4601-030-022-5270, Document Control Number 04800-030-0126) is dated June 1995. Also reviewed was a related item received via FAX transmission on January 31, 1996, from EPA Region III Project Manager Mr. Fred Mac Millan titled: "Section 10, Palmerton Zinc Site - Site Materials". This material appears to be an addendum to the "Final Phase II Bioavailability Studies Sample Preparation and Analysis Report" which is specific to the Palmerton Zinc Superfund site. Other materials reviewed include:

2. *Experimental Lead Toxicosis in Swine*, by E.D. Lassen, DVM, Ph.D. and W.B. Buck, DVM, M.S., which was published in American Journal of Veterinary Research, Vol. 40, No. 10 (pp. 1359 - 1364), October, 1979.

3. *Environmental Zinc and Cadmium Pollution Associated With Generalized Osteochondrosis, Osteoporosis, and Nephrocalcinosis in Horses*, by D.E. Gunson, BVSC, Ph.D.; D.F. Kowalczyk, VMD, Ph.D.; C.R. Shoop, VMD; and C.F. Ramburg, Jr., VMD, which was published in the Journal of the American Veterinary Medical Association, Vol. 180, No. 3, Pages 295-299, February 1, 1982.

4. *The Merck Veterinary Manual, Seventh Edition*. 1991. Page 1674, discussion on Lead Poisoning.

5. *Comparative Anatomy of the Vertebrates, Fourth Edition*. by George C. Kent. Chapter 11, Digestive System, Page 253, discussion on Exocrine Pancreas. Published by C.V. Mosby Company, Saint Louis, 1978.

6. *Van Nostrand's Scientific Encyclopedia, Eight Edition*. Douglas M. Considine, Editor. discussions on the Human Digestive System, Pages 957-958; the Digestive System of Other Life Forms Including Ruminants, Pages 959-960; and Lead in Biological Systems-Toxicity, Pages 1863-1864. Published by Van Nostrand Reinholdt, New York, N.Y. 1995.

7. *Revised and Partially Updated Draft - Toxicological Interactions of Cadmium, Lead, and Zinc: A Case Study for Mixtures/Human Health Risk Assessment*. Prepared by: Joan T. Colman, William L. Ruoff and Fernando T. Llados, from the Environmental Science Center, Syracuse Research Corporation. Submitted to the National Center for Environmental Assessment, U.S. Environmental Protection Agency, Cincinnati, Ohio. Dated September 27, 1995. 76 pages.

In general, these ancillary materials were reviewed to compare the protocol of the subject study with previous similar studies, to gain a better understanding of the effects of metals toxicity on humans, pigs and other domestic animals, and to identify similarities and differences between the anatomy and physiology of human and swine digestive systems.

A computerized literature search was conducted utilizing the 1975 - 1994 Congressional Information Service, Inc. Both relevant subject and author database categories were explored, but only remotely related published peer-review articles were produced by the Service. Many of the articles listed were published in journals that are not available at any local libraries. Of the 17 articles that came up on the database, 14 involved pigs, but only 4 investigated the effects of metals on pigs, and only two of these investigated lead as a contaminant of interest. In the related authors category, only four (4) articles were identified by the two (2) authors entered: Dr. Stan W. Casteel, D.M.V., Ph.D. (Author of the subject study protocol), and E.D. Lassen, D.M.V., Ph.D. (Author of *Experimental Lead Toxicosis in Swine*, item #2 above). One of these articles was authored by Dr. Casteel, a two (2) page report published in 1985 in the Journal "Veterinary Medicine" titled: *Toxaphene and Poisoning of Swine*. The other three articles were authored by Dr. Lassen, and they all involved work with Llamas, not pigs.

The list of references cited by EPA in the document titled: *Revised and Partially Updated Draft - Toxicological Interactions of Cadmium, Lead, and Zinc: A Case Study for Mixtures/Human Health Risk Assessment* was also reviewed. Some of these studies evaluated the direct toxic effects of heavy metals exposure on target organs or organ systems, but there were also many studies that investigated binary and multiple metal interactions and the possible protective effects of dietary vitamins and minerals such as zinc. As would be expected, there have been many studies conducted examining the effects of exposure to heavy metals on rodents such as rabbits, rats and mice. The literature cited includes at least as many studies involving humans (many of which are smelter workers or other occupational exposure scenarios) as rodents, but there was only one study cited that specifically involved pigs. One article cited that may provide important information regarding the questionable suitability of young pigs as test subjects (or at least as comparable test subjects for evaluating the bioavailability of heavy metals to humans) is: *Characteristics to consider when choosing an animal model for the study of lead bioavailability*, by C.P. Weis and J.M. LaVelle (Chem. Speciat. Bioavail. 3(314): 113-119. 1991). If EPA places considerable weight on the *Systematic Availability of Lead to Young Swine* study as part of the Palmerton OU-3 risk assessment, the PCCE may wish to request a review of the above-referenced paper by Weis and LaVelle as a follow-up or elaboration of this review.

The Project Manual and the Project Notebook (Revision 1) for *Systematic Availability of Lead to Young Swine from Subchronic Administration of Lead-Contaminated Soil (Phase II)*, are technical government documents which include terms, phrases and acronyms that, though deeply entrenched in the scientific/regulatory literature, are otherwise unknown to the lay person or impart a different meaning than would be inferred from the vernacular. This is the case with many scientific/regulatory government documents which employ terms that are contextually specific, but can have multiple meanings (i.e. common, scientific and regulatory meanings) or have evolved their own meanings through the process of integrating scientific principles into the political/regulatory process. However, the subject document is technically complex and relatively well written, so in many instances the most efficient way to accurately relate what has been accomplished to date, and the intent of future studies, is through exact quotation.

To better serve the PCCE membership, and in accordance with the primary intent of the EPA Technical Assistance Grant, a section titled Definitions of Specific Terms or Words has been included at the end of this review. Not all of the terms and words defined in this section are included in the same reference documents, so the source for each definition is identified. Also, because some of the terms and words are combined forms and/or have evolved their own meanings, as described above, it is necessary to infer the intent with which the term was applied within the context of the document under review.

REVIEW

The *Protocol for Systemic Availability of Lead to Young Swine from Subchronic Administration of Lead-Contaminated Soil (Phase II)* begins with a BACKGROUND section (Section 1) which provides an historical overview of efforts by EPA Region VIII to identify the various factors that effect the bioavailability of environmental lead and other metals of toxicological concern. The basis for EPA Region VIII's efforts is their **hypothesis** (emphasis is mine) that in addition to physiological differences, the bioavailability of toxic metals, especially lead, is also influenced by geochemical and geophysical mechanisms. EPA Region VIII is investigating if it can quantify differences in the bioavailability of different geochemical and geophysical states of lead (and possibly other metals), so that reasonable and appropriate remedies, that reduce the risks of childhood lead exposure, can be selected for a variety of Superfund sites with soils and other media impacted by mine wastes (no mention is made of smelter sites, but it is presumed that these studies were designed or modified to address all EPA Superfund sites with inorganic lead contamination).

The Protocol, which is the subject of this review, is Phase II of what appears to be long-term ongoing research by EPA Region VIII into quantifying the bioavailability of toxic metals, especially lead. The Phase I study, which EPA Region VIII previously completed over a period of approximately 5 years, used young pigs to develop an animal model for measuring the **relative** and **absolute** (emphasis is theirs) bioavailability of various lead-contaminated materials. The Phase I study involved exposing young swine to lead acetate or lead in test soil, either orally or intravenously, for 15 days, and then determining the level of lead absorption into blood, soft tissue, and bone.

The Protocol BACKGROUND section reports the following results of the Phase I study:

1. The swine model is an experimentally useful and physiologically plausible model for estimating lead uptake into young children;

2. There is good reproducibility in measured values of lead in blood and tissue, both within and between experiments;

3. The level of lead in the blood increases as a function of time after exposure begins, and appears to approach a plateau after about 14 days of exposure. Also, the level of lead in the blood, measured either as area-under-the-curve or as the pseudo-steady state level, is a **non-linear** function of administered oral dose, both for soluble lead salts (lead acetate) and for lead in test soil (i.e. as the dose is decreased, the percentage of administered lead absorbed into the blood increases) and;

4. The amount of lead present in soft tissues (liver, kidney and cortical and trabecular bone) after 25 days of exposure appears to be an approximately **linear** function of administered dose, both for soluble lead salts (lead acetate) and for lead in test soil (i.e., a linearly higher percent absorption is recorded as the dose increases). Preliminary evaluation of various intravenous (iv) doses used in different phase I experiments shows a similar trend towards linearity of PbB (blood lead) with increasing doses, but this relationship is still uncertain

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The introduction to Section 2, titled: PHASE II OF THE LEAD BIOAVAILABILITY STUDY states in the second paragraph, "...the entire Phase II project is a progressive outgrowth of several years of prior applied research performed by EPA during Phase I and earlier. Therefore, the Phase II design, QAPP, and SOPs (standard operating procedures) are largely simple refinements of the Phase I characterization studies and should require little modification for the purpose of application of the swine model to evaluate bioavailability of Regional soil-lead at Superfund sites. Moreover, there is a strong need to maintain consistency between Phases I and II to demonstrate reproducibility and confidence in the swine model as it begins to be applied beyond the characterization stages."

Section 2.1 states the EPA Phase II Lead Bioavailability study was developed to meet the following 4 objectives:

1. To firmly characterize the dose dependence and time dependence of the biological responses to lead exposures initially observed in Phase I studies.

As related by item #3 of the results of the Phase I study above, EPA Region VIII has observed that there is a non-linear (i.e. **not** 1:1, 1:2, etc.) relationship between the oral dose administered and the blood lead level. EPA believes that the non-linear response is due either to characteristics of the absorption process, or to non-linearities in the biological response to lead. EPA thinks that it is physiologically more probable that the absorption process is the controlling factor, and will design a study to test their hypothesis.

2. To establish a quantitative or semi-quantitative understanding of the effect of fed vs fasted state on the GI (gastro-intestinal) absorption of environmental lead.

The purpose of this aspect of the Phase II study is to quantify, as best as possible, how food in the stomach affects the bioavailability of lead via the oral exposure pathway. As Dr. Rufus Chaney testified at the July 29, 1994 Palmerton Scientific Symposium, lead absorption in the gastro-intestinal (GI) tract is less efficient in a fed vs. a fasted state. Dr. Chaney's testimony focused on his understanding that food in the GI tract will neutralize some of the acidity that is characteristic of the digestive juices of a normal stomach. Since many heavy metals are acid soluble, neutralizing the acidity will make the metals less available for absorption. Dr. Chaney also testified that an individuals nutritional status (i.e. the presence or absence of nutritional deficiencies) is also a key factor that influences the effects of heavy metal exposure.

According to *Van Nostrand's Scientific Encyclopedia,* the digestive juices of the human stomach are highly acidic in contrast to the alkaline secretions of the intestine (pg. 957), which results in a neutralizing effect. Acidity in the stomach is the result of hydrochloric acid (pH 1-3) which is secreted by parietal cells in the stomach lining, but the alkaline (pH 7-8.2) secretions of the small intestine originate mainly from the pancreas and the liver. The intestine is the organ where most absorption occurs, while the stomach is primarily a digestive organ (i.e. it functions to breakdown material before it enters the intestine for adsorption). It is worth noting that lead is soluble in both acidic (especially nitric and organic acids) and basic (sodium hydroxide and other alkalies) solutions, but is least soluble at or near a neutral pH.

3. As requirements and resources permit, fill in other critical data gaps (applied investigations, not basic research) that provide useful model information to enable better understanding and application of the results from the following part 2 studies on site-specific metal uptake and associated health risks.

   Three pilot studies were proposed as part of this objective:

   a) a pilot study to determine depuration kinetics as a possible improved endpoint to assess bioavailability of soil lead, and which may lead to further refinement in the main standard unit studies under part 2;

   b) a pilot study to assess the influence of the dosing vehicle (a low-lead feed preparation) on absorption of lead by comparing Pb absorption following oral gavage vs oral vehicle administration of the same lead dose; this pilot study would also incorporate the ability to determine any effects of smaller vs medium and larger particle size (based upon equal percentages of lead mass for <250 um soil fractions) on the absorption of lead in the immature swine model; and

   c) Interspecies variability in lead absorption under the experimental conditions employed (e.g., immature rats and/or other resistant vs sensitive species as compared to the standard pig model) to improve confidence in extrapolations.

4. (the main objective and overall purpose of Phase II): To establish dose dependence and time dependence of lead absorption across the GI tract of the immature swine model for a wide spectrum of fully characterized environmental media in region VIII.

To recapitulate the **hypothesis** described in the BACKGROUND section (page 4 of this review), EPA Region VIII believes that different types of contamination and lead contaminated media have different bioavailability characteristics. The primary goal of this investigation is to quantify differences in bioavailability, so that reasonable and appropriate remedies can be selected that reduce the risks of childhood lead exposure.

Section 2.2 of the Protocol identifies EPA's Conceptual Model for lead absorption. The first step is the transformation from solid lead-bearing grains to a more bioaccessible state. It is not known if the more bioaccessible state is as dissolved lead ions, or as minute particles that can contact the gastrointestinal epithelium (i.e. the intestinal lining). The second state is absorption from the gastrointestinal tract to the blood. Since it is not known whether the lead is in a solid or dissolved state, the actual mechanism of absorption is also not known. EPA believes that the process is similar to the divalent cationic transport systems that allows for the absorption of calcium. Three possible processes are identified: Active, which EPA perceives as saturable, resulting in a non-linear dose response; passive, which EPA perceives as non-saturable, resulting in a linear dose response; and other, such as pinocytosis, in which the cell wall surrounds or engulfs the particle thereby allowing it to enter the cell protoplasm.

Section 2.3 outlines the mathematical methods that will be employed for calculating the Relative Bioaccessibility Factor (RBAF). In this section the Protocol authors express their justification for selecting weanling swine for comparison with the target population (young children). These are: The immature swine is similar in physiologic age and body weight to the childhood population, and allows repeated blood sampling for blood lead analysis without fear of developing anemia. At this point the authors recognize that there may be some differences between lead bioavailability in young pigs and children, but state that the Phase II study was designed to minimize (experimentally control) the impact of these possible differences on 1) absorption and 2) tissue response, and will instead focus on estimating the amount of lead that is converted to a bioaccessible state. This leads to a description of the method for calculating the Relative Bioaccessibility Factor (RBAF).

Basically the RBAF is an averaged ratio of the bioaccessibility of various lead contaminated media to the bioaccessibility of lead acetate. EPA assumes that because lead acetate is a soluble salt, that it is fully bioaccessible. An assumption is also made that the RBAF is a constant. For example if the dose response from one unit of lead acetate is the same as for two units of test soil, then the dose response of two units of lead acetate would be the same as for four units of test soil. The authors conceded that this assumption may also be faulty, especially at high concentration doses, and discuss the possible need to base the final model on selected values that are the most physiologically relevant for children.

Section 2.4 of the Protocol discusses the selection of a biological response or indicator for calculating the Relative Bioaccessibility Factor (RBAF). Because there may be differences between the quality of the data for different indicators (i.e. sensitivity, linearity, signal to noise ratios, etc.), EPA has identified six (6) responses that they will measure and compare.

These include:

1. Area under the blood lead vs. time curve (AUC); (this is a statistical measure of how fast and how much of the administered lead dose ends up in the blood. Presumably the greater the area under the curve, the faster the response and/or the greater the percentage absorbed)

2. Depuration (washout) kinetics following subchronic central compartment loading; (apparently this is to measure how fast and how much the blood lead level decreases after exposure)

3. Initial rates (slope of PbB vs time curve) of absorption into the central compartment; (this appears to be similar to response 1. above, but this is a measure of the slope of the curves instead of the area under the curve)

4. Pseudo-steady state blood lead value (average after 14 days of dosing); (Apparently the assumption here is that the blood lead levels after 14 days of exposure will reach a plateau. This is conclusion 3) of the Phase I study.)

5. The level of lead in soft tissue (kidney, liver) at study termination; (remember that soft tissue concentrations were found to be related to dose) and

6. Lead levels in a single, consistently collected/prepared, reporter bone (right femur).

The data from the six (6) biological responses can be applied to obtaining reliable estimates of the absolute absorption of lead from various sources. To achieve this objective, the biological response of ingested lead will be compared with the biological response of lead that is administered systematically (presumably through intravenous injection since gavage still requires gastrointestinal absorption). By comparing the biological responses of oral and systematic administrations, a ratio can be calculated called the Absolute Absorbed Fraction (AAF). However, the AAF ratio is only valid if there is a linear dose-response relationship. Otherwise, the AAF would be a function of the modeled nonlinear dose-response relationship.

Section 3 describes what are called the Phase II Part 1 Studies, which correspond to objectives 1 through 3 for Phase II as described earlier in section 2.1. Section 3 is where the Protocol moves beyond the conceptual discussion and into the actual methodology for achieving the objectives identified in Section 2. Section 3.1 describes the methodology for evaluating the linearity of biological responses (see objective #1). This will be accomplished by administering the lead systemically (by intravenous injection or an osmotic pump), and then measuring the blood lead level as well as other biological responses. The Protocol states that this study can also be used to determine separate estimates of the magnitude of the biological responses to various levels of systematically absorbed lead.

Section 3.2 describes the methodology for determining lead absorption in a fed vs. a fasted state, which is to be accomplished by feeding the pigs before, after and during exposure to lead (Objective 2). This experiment will also involve two control groups, one control group will receive low lead feed only, while the other control group will receive an intravenous dose of lead acetate. All other test subjects will be given split oral doses of lead acetate, before, during and after feeding.

Sections 3.3, 3.4 and 3.5 describe the methodologies for achieving Objectives 3 a),b), and c). Objective 3 a) is to determine whether the "loading" or the "loaded" blood lead state is a better biological endpoint for determining lead bioavailability. The dosing and sampling schedules are described, but the conceptual methodology for these studies were never clearly identified. Presumably, the loading endpoint is a measure of how fast (dose vs time) and how efficiently (dose vs percent increase in blood lead level) lead accumulates in the blood. By contrast, the loaded endpoint is presumably a measure of how quickly lead leaves the bloodstream after exposure is stopped. As far as a measure of bioavailability is concerned, both endpoints would seem useful as risk assessment tools, and it is difficult to understand why one endpoint needs to be selected over the other.

Section 3.4 describes the methodology for determining what influence the vehicle and the particle size have on lead bioavailability. Once again the dosing schedules are presented in a table, but the conceptual basis is not clearly explained. It is difficult to determine how particle size will be evaluated, since all oral doses will be with particles less than 250 micrometers in size. Further, the vehicle is never clearly defined.

Section 3.5 describes the methodology for determining the variability between pigs and other animals in lead bioavailability studies. The animals to be investigated include rats, rabbits, calves/lambs, dogs/monkeys, and pigs. Each animal will be administered the same concentration of lead acetate per day per kilogram of body weight (225 ug/kg/day). Each species of animal, except for dogs and monkeys, will be sacrificed after 21 days, and their tissues examined.

Section 4 addresses the main emphasis of the Phase II study (objective 4), which is a comparison of the bioavailability of various lead contaminated media (mine wastes and presumably smelter emissions from Palmerton) with lead acetate (which is assumed to be 100% bioavailable). This section states that if any of the media tested (mine wastes and smelter emissions) is found to be significantly less bioavailable, then quantitative adjustments will be made to the risk assessment for those materials. It is also stated that by correlating the RBAF's of various materials with specific geophysical characteristics, it will be possible to determine the relative bioavailability associated with certain physical-chemical properties. This information will then be used to assess the bioavailability of other lead contaminated wastes that were not included in this swine model study.

Section 4 includes two parts, 4.1 and 4.2. Both sections seem to address determination of the oral dose-response. While Section 4.1 involves a comparison of lead acetate with various lead contaminated soils, Section 4.2 appears to be a comparison of various lead contaminated soils from EPA Region VIII. It is curious that the dosing schedule for Section 4.2 (Table 9) also includes a lead acetate test group. Consequently, it was not clear what the conceptual design difference is between the two parts of Section 4.

The Protocol ends with a section titled, underlined, and in large font text **ADDENDUM TO PROTOCOL**. Apparently there is an entity called the Region VIII Lead Absorption Technical Advisory Committee (TAC), that has decided the Phase II Protocol should be revised "...in the interest of efficient use of time and available resources ...". The Addendum is a consolidation of the original study design so that certain study components can be run concurrently. Apparently this will require that "... pilot studies of importance to adequate scientific interpretation of the Phase I and Phase II work as outlined in Tables 2, 3 and 4 of the Study Protocol will be reduced in scope...". Table 2 is the schedule for the study required to meet Objective #1, Table 3 is the schedule for the study required to meet Objective #2, and Table 4 is the schedule for the study required to meet Objective #3. The impact of this Addendum on the quality of the data or the sensitivity of study will be difficult to evaluate until the results of the study are published and carefully reviewed.

The item received via FAX transmission on January 31, 1996, from EPA Region III Project Manager Mr. Fred Mac Millan titled: "Section 10, Palmerton Zinc Site - Site Materials" appears to be an addendum to the "Final Phase II Bioavailability Studies Sample Preparation and Analysis Report" which is specific to the Palmerton Zinc Superfund site. What this means is that samples from Palmerton have been included in the EPA Region VIII study, but it is not known if any of the material from Palmerton was actually fed to any of the swine test subjects. The cover letter from Gerald L. Almquist, Senior Project Manager for Roy F. Weston, Inc., discusses speciation studies of two new samples from Locations 2 and 4. Page 10-3, paragraph 2 states: "...EPA Region VIII made a decision to utilize samples from locations 2 and 4 for the bioavailability study.", but it is not made clear exactly how these samples were used. Possibly the Palmerton samples are only being characterized so that their physical-chemical characteristics can be compared to the physical-chemical characteristics of soil from another site with a calculated Relative Bioaccessability Factor (RBAF).

This methodology was described in Section 4 of the Protocol where it was stated that if any of the media tested (mine wastes and smelter emissions) is found to be significantly less bioavailable, then quantitative adjustments will be made to the risk assessment for those materials. Further it is stated: **"...by correlating the measured RBAF of various materials with the geophysical characteristics of the test materials, it may be possible to begin to identify physical-chemical properties that are associated with both relatively high and low bioavailability. This, in turn, will allow for improved risk assessment for lead-contaminated wastes even when a related material of concern has not been tested in the swine model."**

Section 10 states that sampling was conducted on August 28, 1995 by Richard Tobia and Dennis Kalnicky of REAC, Fred Stroud from U.S. EPA/ERT, Fred Mac Millan from U.S. EPA Region III, and Mark Steidinger from Zinc Company of America. Five (5) locations were screened for average lead concentrations greater than 1,500 mg/kg, and four of these locations were sampled. Samples were collected from the top 1 to 2 inches of four 1-foot square areas (collected from one 2-foot by 2-foot square area from each location), with clean stainless steel trowels. All sample material was qualitatively characterized as dry, dusty leaf debris and organic soil. **"At the end of the day, each bag was subsampled for metals analysis, which was performed by Horsehead Industries"** (page 10-3). After the samples were delivered to the WESTON Lakewood Colorado office, EPA Region III made the decision to utilize samples from locations 2 and 4 for the bioavailability study. The individual from EPA Region III who made this important decision, and the justification for their decision is not identified in the report.

Contract Lab Program analysis was conducted by EPA Region VIII's Routine Analytical Service for total metals on samples collected at locations 2 and 4. These results are reported in Table 10-1 for location 2 and Table 10-2 for location 4. Two additional figures, apparently the results of the speciation study, were also included with the Section 10 report, but are unreadable. Among the metals of interest, samples collected from Location 2 had an arsenic concentration of 110 ppm, a cadmium concentration of 195 ppm, a lead concentration of 3230 ppm, and a zinc concentration of 6500 ppm. Two other metals that may be of interest from these samples are manganese (6320 ppm) and iron (25,900 ppm). Analysis of samples from Location 4 yielded the following results: arsenic 134 ppm, cadmium 319 ppm, iron 26,700 ppm, lead 2150 ppm, manganese 9230 ppm, and zinc 19,100 ppm.

According to the map provided, Location 2 is in the east side of Palmerton, north of the intersection of Princeton and 8th street. Location 4 is in the west side of town, north of Edgemont, probably a short distance northwest of the Firehall where the "Scientific Symposium" was held. The map provided includes symbols (not numbered locations) which indicate possible other sample locations, one on Blue Mountain immediately south of the East Plant, and another on the east side of town, between Princeton St. and Towamensing Trail. No other information was made available, indeed no information at all, about soils collected from the other locations.

There are six (6) other similar Sections in a Chapter of the **PROJECT NOTEBOOK** titled: FINAL PHASE II BIOAVAILABILITY STUDIES SAMPLE PREPARATION AND ANALYSIS REPORT. These six other Sections report on the sample collection and analysis at the following Superfund sites: Kennecott NPL Site, Salt Lake City Utah (Section 3); Jasper County, Missouri, NPL Site (Section 4); Murray Smelter NPL Site, Murray City Utah (Section 5); Smuggler Mountain NPL Site, Aspen, Colorado (Section 6); Silver Bow Creek/Butte Area NPL Site, Butte, Montana (Section 7); and the Arkansas Valley (AV) Slag Pile/California Gulch NPL Site, Leadville Colorado (Section 8). Because the Palmerton sampling is titled Section 10, it appears as if there is another Superfund site that was sampled and characterized, but information on this site was not provided.

Of the six (6) sites, other than Palmerton, for which metals analysis results were provided, all but two sites; Smuggler Mountain, in Aspen Colorado, and Kennecott Utah, have also been impacted by smelter emissions (recall that the Protocol discussed mine wastes, not smelter wastes). Although the EPA reports do not state the source, the information provided seems to indicate that Kennecott is primarily a smelter site. Because EPA believes that it will be possible to apply experimentally determined RBAF's (from the sites investigated in this study) to other sites (not included in this study), the characteristics of various lead bearing materials at different sites should be investigated. Below is a brief description of the physical and chemical characteristics of the material sampled, at each site, for use in the pig study. A comparison to the information provided for the Palmerton site is included.

Kennecott NPL Site, Salt Lake City Utah (Section 3): Possibly a smelter site (type of facility not identified) based upon particle size and Frequency and Relative Mass samples. Particle size distribution very small (most from 0 to 5 microns). Iron-lead phosphate levels and lead phosphate levels high in all samples; manganese lead oxide levels also high in low lead samples. Two types of samples collected and analyzed, high lead (6,330 ppm) and low lead (1590 ppm). Relative to Palmerton (110-134 ppm As), arsenic concentrations are comparable for high lead samples (149 ppm), but somewhat low for low lead samples (51.20 ppm) at Kennecott. Cadmium concentrations at the Kennecott NPL Site (8.7 to 4.2 ppm Cd) are much lower than at Palmerton (195 to 319 ppm Cd). Lead levels at Kennecott (high lead sample of 6330 ppm and low lead sample of 1590 ppm) are comparable to Palmerton (3230 to 2150 ppm Pb). And zinc concentrations at Kennecott (903 ppm Zn) were much lower than at Palmerton (6500 to 19,100 ppm Zn).

Jasper County, Missouri, NPL Site (Section 4): A Smelter, and possibly an Ore Mill. Particle size distribution is small. High relative mass and frequency, among some samples, of Cerussite (lead carbonate) mineral particles characteristic of lead bearing ores found in places such as Phoenixville, Pennsylvania; Joplin, Missouri; and Leadville, Colorado. Other samples have a high relative mass and a high frequency of slag particles. Four types of samples were collected in Jasper County: High Level Smelter Wastes (HL Smelter), High Level Mill Wastes (HL Mill), Low Level Yard Samples (LL Yard) and Low Level Yard Sample Duplicates (LL Yard Duplicates). Relative to Palmerton (110-134 ppm As), arsenic concentrations are low for all samples (9.1 to 25.1 ppm As). Cadmium concentrations at the Jasper County NPL Site (33.7 to 188 ppm Cd) are generally lower than at Palmerton (195 to 319 ppm Cd). Lead levels at Jasper (10,800 to 3850 ppm Pb) are much higher than at Palmerton (3230 to 2150 ppm Pb). Finally, zinc levels at Jasper (10,000 to 54,600 ppm Zn) range from comparable to much higher than samples collected at Palmerton (6500 to 19,100 ppm Zn).

Murray Smelter NPL Site, Murray City Utah (Section 5): A smelter site. Overall particle sizes are more evenly distributed than at the Kennecott or Jasper sites, with high particle counts at 5 and 150 micron sizes. The greatest frequency of lead particles is slag, with lead oxide comprising the greatest relative mass of lead particles. Relative to Palmerton (110-134 ppm As), arsenic concentrations are high for composite samples (710 to 680 ppm As). Cadmium concentrations at the Murray City NPL Site (30.9 to 28.9 ppm Cd) are much lower than at Palmerton (195 to 319 ppm Cd). Lead levels at Murray City (11,700 to 11,300 ppm Pb) are much higher than at Palmerton (3230 to 2150 ppm Pb). Finally, zinc levels at Murray City (49,500 to 48,200 ppm Zn) are much higher than samples collected at Palmerton (6500 to 19,100 ppm Zn). An interesting twist to the Murray City analysis is that EPA compared the quantity of liberated to included lead, a possible bioavailability factor.

Smuggler Mountain NPL Site, Aspen, Colorado (Section 6): This site is identified as a mine site, although it is likely that other types of processing occurred at the site as well. Composite samples were collected from two locations, a group of residential properties, and from the vicinity of the Racquet Club property, which is referred to as "the berm". In general particle sizes are small, especially from the residential properties, which are overwhelmingly less than 10 microns in size. The quantity of particles from "the berm" site are still mostly in the 5 to 10 micron size range, but extent all the way to the greater than 250 micron range. Based on frequency of particles, iron-lead oxide is the most prevalent lead compound at both residential and berm sites, with Cerussite having the second highest frequency. By a wide margin, Cerussite comprises the highest relative mass of all lead Bering compounds at both sample locations. Compared to Palmerton (110-134 ppm As), arsenic concentrations are low for both residential and berm samples (16.7 to 66.9 ppm As). Cadmium concentrations at Aspen (47.4 to 41.9 ppm Cd) are much lower than at Palmerton (195 to 319 ppm Cd). Lead levels at Aspen (3,870 to 14,200 ppm Pb) are both comparable (residential) and much higher (the berm) than at Palmerton (3230 to 2150 ppm Pb). Finally, zinc levels at Aspen (4110 to 6580 ppm Zn) are comparable though somewhat lower than samples collected at Palmerton (6500 to 19,100 ppm Zn).

Silver Bow Creek/Butte Area NPL Site, Butte, Montana (Section 7): This site has both a mine and a smelter associated with the levels of lead contamination. All sites sampled at the Silver Bow Creek/Butte Area NPL Site were composited into one sample for analysis. This may possibly explain why particle sizes are more evenly distributed than at other sites, with most particles ranging from 5 to 100 microns in size. The primary components of lead bearing materials based on frequency of occurrence are iron-lead sulfate, manganese-lead oxide, and Anglesite, (a naturally occurring lead sulfate mineral). Ranked according to mass, lead contamination at the Silver Bow Creek/Butte Area NPL Site is primarily composed of Anglesite, Galena, iron-lead sulfate, and manganese-lead oxide. Compared to Palmerton (110-134 ppm As), arsenic concentrations are slightly higher in Butte samples (226 to 251 ppm As). Cadmium concentrations at Butte (42.2 to 43.1 ppm Cd) are much lower than at Palmerton (195 to 319 ppm Cd). Lead levels at Butte (8530 to 8640 ppm Pb) are both considerably higher than at Palmerton (3230 to 2150 ppm Pb). Finally, zinc levels at Butte (12,100 to 12,500 ppm Zn) are comparable to samples collected at Palmerton (6500 to 19,100 ppm Zn).

The Arkansas Valley (AV) Slag Pile/California Gulch NPL Site, Leadville Colorado (Section 8): The sample media collected from the Arkansas Valley (AV) Slag Pile/California Gulch NPL Site is all water quenched fines (slag), so it is presumed to be entirely composed of smelter wastes. Not unlike the material from the Butte Site, the particle size distribution of samples from Leadville is relatively evenly distributed, with the majority of particles in the 5 micron size, a second peak at the 150 micron size, and fairly even representation for all other size classes, except for 20 microns, which is the least prevalent. As would be expected, the Relative Frequency of particles was predominantly slag, with Relative Mass being comprised mainly of lead oxide and lead-arsenic oxide. Compared to Palmerton (110-134 ppm As), arsenic concentrations are much higher in Leadville samples (1050 ppm As). Cadmium concentrations at Leadville (12.8 ppm Cd) are much lower than at Palmerton (195 to 319 ppm Cd). Lead levels at Leadville (10,600 ppm Pb) is considerably higher than at Palmerton (3230 to 2150 ppm Pb). Finally, zinc levels at Leadville (67,300 ppm Zn) are much higher than samples collected at Palmerton (6500 to 19,100 ppm Zn).

DISCUSSION

Many factors need to be considered when reviewing the Protocol of a study such as this. The first factor that should be addressed is: What is the intent of the study? Although these are addressed in the discussion of Objectives, faithfully recapitulated on pages 5 and 6 of this summary, they do not really become apparent until Section 4.1 of the Protocol. It is at this point where the authors of the Protocol bare their ambitions to the fullest extent. In short, the pig study is designed to:

1. Determine the relative and absolute bioavailability of various lead bearing wastes to human children by experimentally determining the bioavailability to pigs that are the same age and weight.

2. Characterize the Relative Bioaccessibility Factor (RBAF) for various combinations of lead compounds, so that the RBAF at other sites can be determined by simply comparing the lead species present at one site with the lead species present at the site of interest.

This is a fantastic and extraordinary scientific initiative, that has taken 5 or more years to develop, and will no doubt cost hundreds of thousands, if not millions of dollars to complete. With all of the government mandated Standard Operating Procedures (published in the Federal Register no less), Quality Assurance Project Plans, and many of the largest and most respected environmental consulting firms in the country out taking samples; the results of this study are certain to produce powerful and conclusive data that will allow environmental risk managers to make better decisions toward protecting the health and safety of our children who are exposed to environmental lead contamination, right? There may be another objective to this study that is not so clearly stated.

Remember the ATSDR study titled: "Biological Indicators of Exposure to Cadmium and Lead, Palmerton, Pennsylvania (Parts I and II)? The sub-section titled **Rational for Study Design**, in the **METHODS** section of the Part I Final Report states: **"The specific aim of this study was to determine whether people who lived near the contaminated areas in the town of Palmerton and the adjoining community of Aquashicola (target area) had higher levels of cadmium and lead than residents of a presumably uncontaminated comparison area."** The Draft for Public Comment version of the same report, released in April of 1993, included the same sentence, but without the qualifier **presumably**. Read with a discriminating eye, several basic conclusions were reached by that study:

1. "Blood lead levels in the target population (Palmerton and Aquashicola) were not different from those in the comparison population (Jim Thorpe)." (Part I Report, Page 43, conclusion #1.)

2. "Among Children under 6 years of age, 23% in the target area and 27% in the comparison area had blood levels greater than or equal to 10.0 *u*g/dL." (Part I Report, Page 43, conclusion #2.)

3. "Blood lead was not found to be associated with any of the biomarkers examined." (Part II Report, Page 19, #3.)

Are these results surprising?

All good intentions aside, the ATSDR "Biological Indicators" study had one critical flaw to the study design that continued through various drafts and comment periods, but was never corrected. Jim Thorpe was not a good comparison community because it too was contaminated with lead. Consequently, the specific aim of the Part I study could not be attained. Should EPA have been surprised? With a known geologic source of natural radiogenic lead contributing to the soil profile; and with the Tonolli Facility, a now defunct secondary lead smelter and NPL site, located just a few miles upwind in the narrow Nesquehoning valley, it is hard to believe that no one checked to see if Jim Thorpe was also contaminated before spending all that money on the ATSDR study.

To be critical, it seems that, for whatever reason, government mandated studies often carry their own inertia, that allows them to continue through seemingly endless iterations, drafts, and public comment periods to reach conclusions that are either invalid or inconclusive. Take the ATDSR study for example once again. One of the conclusions reached to explain the lack of epidemiological indicators was that some of the biological end points examined may not have been sufficiently sensitive. It was interesting to note that many of the hematological effects evaluated by Thawley et. al. (refer to *Revised and Partially Updated Draft - Toxicological Interactions of Cadmium, Lead, and Zinc: A Case Study for Mixtures/Human Health Risk Assessment*, section 5.2, page 14) were also evaluated by ATSDR in Palmerton and East Jim Thorpe (e.g. blood hemoglobin, mean corpuscular volume, and mean corpuscular hemoglobin), with a similar no measurable effect conclusion. The Thawley study was published in 1977; although it probably was not included as part of the literature review, because it used rats as test subjects. This leads to the next subject of discussion.

In the Background section of the pig study protocol, it is stated that EPA determined through the Phase I study that "...The swine model is an experimentally **useful** and physiologically **plausible** model for estimating lead uptake into young children". Without having thoroughly reviewed the Phase I study methodology, data analysis and report conclusions, it is not possible to determine why the investigators reached this conclusion. Further, the Protocol authors do not reference any peer-reviewed primary research reports to

support their conclusion. One reasonable justification is provided in section 2.3 (page 4, last paragraph), of the pig protocol: **"... The immature swine has been selected as the test species for both Phase I and Phase II studies because it is believed that the gastrointestinal physiology of the young swine is a plausible model for the human child. The immature swine is similar in physiologic age and body weight to the childhood population of interest and affords easy serial blood sampling without risk of exsanguination or anemia as in smaller laboratory animals."** The concern about the risk of exsanguination seems justified, but the statements regarding similar gastrointestinal physiology and similar physiological age take a leap of faith.

In two of the documents reviewed, the **plausibility** of the swine model is brought into serious question. First of all, the *Merck Veterinary Manual, Seventh Edition*. 1991. Page 1674, discussion on Lead Poisoning, simply states that pigs are comparatively (in comparison to cattle and dogs) resistant to lead poisoning. But what is the significance of this comparison?

To answer the question of comparative significance, the peer-reviewed journal article titled: "*Experimental Lead Toxicosis in Swine*", by E.D. Lassen, DVM, Ph.D. and W.B. Buck, DVM, M.S., was reviewed. This article was published in the American Journal of Veterinary Research, Vol. 40, No. 10 (pp. 1359 - 1364), October, 1979. Lassen et. al exposed 30 young pigs, 17 to 24 kg in size (as compared to the 10 to 12 kg pigs used to determine the swine model) to various concentrations to lead acetate (orally and interperitoneally) for 13 weeks. The oral Lead dose administered ranged from 4.4 mg/kg to 35.2 mg/kg (dose is reported as lead only, not as lead acetate). Interperitoneal doses ranged from 1.1 mg/kg to 8.8 mg/kg Lead. Note that one of the assumptions of the swine model protocol is that Lead Acetate is 100% bioavailable. This caused blood lead levels in some test animals (dosed interperitoneally) to climb as high as 14,300 *u*g/dl (micrograms per deciliter). Recall that in Human children, a blood lead level greater than 10 ug/dl is considered cause for concern, and a blood lead level above 15 ug/dl indicates a serious exposure problem. Two pigs each from the two groups given the highest interperitoneal concentrations died, and the higher doses did cause more pronounced toxicity symptoms, but one pig each from each group survived the duration of the test. The authors concluded that pigs are extremely tolerant of lead. Does this demonstrate similar physiology?

Pigs are omnivorous mammals, humans are omnivorous mammals; but the similarities between the gastrointestinal tracts of young pigs and human children seem to diverge beyond that point. First of all, there are minor morphological differences between the gastrointestinal tracts of pigs and humans. For example: In pigs, not unlike oxen, the duct of the ventral pancreas loses its connection to the common bile duct, and the entire pancreas drains directly into the duodenum. In humans, as in cats, one of the two ducts is larger, and the other is referred to as the pancreatic duct. The pancreas secretes alkaline fluids that both aid in digestion and help to neutralize some of the acidity from the stomach. Recall that Lead is soluble in both acids and bases. Are there differences between the acidity of pig digestive juices and human digestive juices? The importance of these morphological and physiological differences may or may not be significant, but since most of the absorption occurs in the duodenum, below the pancreatic ducts, it should be properly addressed.

Physiologically, one major difference between weanling swine and human children is probably physiologic age. Anyone who has raised pigs knows that pigs and people develop at different physiological rates. For example, pigs are fully mobile only a few days after birth. Humans, by contrast, can scarcely crawl after 6 month of development, and typically take up to a full year before they are ready to walk. Quite simply, the physiological development of pigs occurs much more quickly.

There are different epidemiological responses between environmental lead exposure to human children, and human adults. Some of this may be due to the fact that the human organs of digestion are not fully developed until the child reaches sexual maturity (puberty). Pigs mature sexually at a much faster rate than humans. In conclusion, the question of physiological similarities and differences needs to be fully addressed before the swine model can be recognized as plausible.

In Section 4 of the Protocol, it is stated that the purpose of Part 2 of the Phase II study is "...to investigate the bioavailable fraction of a variety of materials from mine waste sites (slag, waste rock, tailings, contaminated soils, etc.) to determine if Pb (lead) in any of these materials is significantly less bioavailable than Pb in lead acetate or in other matrices from Region VIII sites." This statement is confusing for several reasons: First, some of the sites sampled for the swine model study are not located in EPA Region VIII, these include Jasper County, Missouri and Palmerton, Pennsylvania. It is assumed that use of the term *"mine wastes"* includes smelter wastes, since most if not all of the Superfund sites sampled are smelter sites, but they are not all mine sites. Recall that the study design assumes that lead acetate is 100% bioavailable. Does this assumption apply to oral administration? Has this been demonstrated experimentally? The 100% bioavailability assumption is not consistent with the experimental results reported by E.D. Lassen et. al. (1979), which demonstrated that blood lead concentrations leveled off after several weeks of oral administration. Furthermore, the results reported by Lassen et.al. are supported by the conclusions of the Phase I Swine Model study, which states that "...the level of lead in the blood, measured either as area-under-the-curve or as the pseudo-steady state level, is a **non-linear** function of administered oral dose, both for soluble lead salts (lead acetate) and for lead in test soil...". Why was this assumption made when it is well known that oral administration of lead acetate is not 100% bioavailable? What is the importance of this assumption for comparing bioavailability among and between media? Does the Integrated Exposure Uptake Biokinetic model (IEUBK), EPA's standard risk assessment exposure model, assume that any lead contaminated media is 100% bioavailable?

EPA plans to establish the Relative Bioaccessibility Factor (RBAF) for each type of material sampled from the various Superfund sites included in the study. The intent is to use the RBAF values to refine the risk assessment and cleanup standards at those sites. If any of the media tested is found to be significantly less bioavailable than lead acetate or other types of lead contaminated wastes, then quantitative adjustments will be made to the risk assessment and cleanup standards for those materials. Furthermore, EPA believes that it may be possible to apply the RBAF values that were determined experimentally to sites that were not included in the swine study (i.e. not determined experimentally). This is to be accomplished by experimentally determining the RBAF's for various types of lead contaminated media (i.e. media with different physical and chemical characteristics), and then applying the RBAF that is appropriate for each lead species found at other sites.

The sample data provided in the **PROJECT NOTEBOOK** chapter titled: FINAL PHASE II BIOAVAILABILITY STUDIES SAMPLE PREPARATION AND ANALYSIS REPORT, as faithfully recapitulated on pages 12, 13, and 14 of this summary review, seem to indicate that there is a great deal of variability between the physical and chemical characteristics of lead bearing wastes at the sites included in the experimental study. Either we can credit EPA Region VIII with selecting sites which represent a broad range of geophysical and geochemical characteristics for lead bearing materials, or the data provided does not represent a large enough sample population to demonstrate significant chemical and physical similarities between sites. If there is not sufficient chemical and physical similarity between sites, it is not possible to establish media specific RBAF's, and the primary purpose of the Phase II study cannot be met.

One obvious similarity between sites is the frequency of various size materials. However, this is likely to be the result of analytical design, sampling bias and sample processing. For example, the particle size distribution is almost always greater for smaller size (<5 microns) particles because more small particles can fit into a sample of a given size than large particles. Consider a blind random sample of one cubic foot of material from along the bank of a stream. Now count the number of individual particles that are in each size classification, using 10 micron intervals. Even if half of the sample **mass** was material greater than 10 microns in size, the **number** of particles less than 10 microns in size would almost certainly be more than 10 times more prevalent. If samples at all sites were collected in the same manner as at Palmerton, sample selection was strongly biased, and not random. Also, since the samples were sieved to remove materials greater than 250 microns in size, it is not surprising that many larger particles were not as frequently encountered. Finally, some similarities are to be expected because of similar geologic sources. However, various types of ores from different geologic sources have been used at Palmerton over the years, representing a broad range of lead species. More recently, the waelz kilning of EAF dust represents an additional source of lead contaminated media that is not likely to be found at other sites.

The analysis of frequency and relative mass lead for various lead containing compounds also exhibited variability in the chemical composition of the samples. Because many of these samples were collected from sites with smelters, some uniformity, especially for oxides of lead, would be expected by chance alone. But generally speaking, the frequency and relative mass ratios of the various lead containing compounds are sufficiently different that one could probably use the ratios to identify the source. Recall that this was one of the methodologies used by EPA's National Enforcement Investigations Center (NEIC) to complete the Hazardous Substances Source Identification Study conducted at Palmerton. There was considerable controversy regarding the validity of the NEIC study, which correlated three types of chemical and physical analyses, to determine the source of lead contamination in Palmerton. Why does EPA think people will believe they can accurately predict the RBAF for specific sites based on speciation, when the NEIC study produced so much controversy.

Another issue that needs to be addressed in this regard is the number and representativeness of samples collected at each site, and the number of samples from each site used to determine the RBAF's. Only four samples were collected at Palmerton. Of these four, only two were actually used. While the chemical and physical characteristics of these samples seem to indicate that they are similar, they cannot represent the full range of materials that people are exposed to in Palmerton. Was there electric arc furnace dust in the samples? Was there material from the cinder pile in the samples? How homogeneous is the cinder pile? Was there lead paint in the samples? Is there a possible antagonistic effect when lead and zinc exposure occur simultaneously? Is there a possible synergistic effect when EAF dust and IRM exposure occur simultaneously? While some of these questions may be dismissed as cynical bantering, they are no more speculative than some of the hypotheses and objectives offered by the swine model and other similar risk assessment studies.

Another question and/or concern expressed by the PCCE membership in Task Schedule #13 involves the issue of multiple exposure pathways. Clearly the swine model addresses only the oral ingestion exposure pathway for soil, and cannot account for exposure related to windborne lead contaminated dust and/or fugitive emissions from current operations. While air pollution control and air monitoring efforts have both improved dramatically in the past couple of years, no system is perfect, and occasional undetected atmospheric releases are bound to occur. In addition, the swine study only addresses oral ingestion of lead contaminated soil, but other lead contaminated media (water, vegetable matter and animal flesh, for example) can also be ingested.

One final item of interest that should be addressed before the results of the pig study are accepted as a contribution to EPA's risk assessment of OU-3. Some design elements of the proposed study remain flexible and are subject to change depending upon the outcome of other/previous study segments. One issue that needs to be addressed in this regard, is the **Addendum To Protocol** that appears at the end of the Protocol section of both the Project Manual and the Project Notebook. The **Addendum To Protocol** section states that the addendum was prepared in the interest of efficient use of time and available resources and at the request of the Region VIII Lead Absorption Technical Advisory Committee (TAC). It may be important to know who the members of the Region VIII Lead Absorption Technical Advisory Committee are, and whether they have considered what impact consolidation of such a complicated study will have on the public involvement process.

EPA needs to recognize that they face a widening credibility gap between themselves and the Citizens of Palmerton because they continue to participate in studies which are unnecessarily complicated and have the outward appearance of being a means to justify relaxation of the cleanup standards. The threshold for neurodevelopmental damage resulting from chronic low level exposure to environmental lead has yet to be firmly established. It is troubling that EPA persists in conducting studies which are designed to justify a relaxation of the cleanup standards when health officials seem to be increasingly concerned with lower levels of blood lead in children.

DEFINITIONS OF SPECIFIC TERMS OR WORDS

b.i.d. - an abbreviation for the latin words "bis in die", which is commonly used in the pharmaceutical trade to mean twice daily. Source: Websters New World Dictionary Of American English - Third College Edition. 1991. Published by Simon & Schuster, Inc. New York N.Y.

Cortical - **1** of a cortex **2** consisting of a cortex **3** involving, or in some way caused by, the brain cortex. Root form Cortex - 1a) the outer part or external layers of an internal organ, as of the kidney or the adrenal glands b) the outer layer of gray matter over most of the brain. Source of both above: Websters New World Dictionary Of American English - Third College Edition. 1991. Published by Simon & Schuster, Inc. New York N.Y. **or** Cortex - an outer zone of any organ or part, as in the mammalian kidney and brain. Source: The Harper Collins Dictionary of Biology, by: W.G. Hale and J.P. Margham. 1991. Published by HarperCollins Publishers, New York N.Y.

Depuration Kinetics - A combined term composed of the words: Depurate - to purify. Kinetics - **1** of or resulting from motion. **2** energetic or dynamic. Source: Websters New World Dictionary Of American English - Third College Edition. 1991. Published by Simon & Schuster, Inc. New York N.Y. Interpretive note: This term in the combined form should mean "the dynamics of purification". This interpretation is reinforced in the Protocol through insertion of the word (washout) within the term. However, it is not clear from reading section 3.3 if this pertains only to changes in the blood lead concentration following each subsequent blood sample, or if factors such as excretion in the feces and urine or storage in tissues such as bone will be taken into consideration.

Exsanguination - Root form is Exsanguine - bloodless, anemic. Source: Websters New World Dictionary Of American English - Third College Edition. 1991. Published by Simon & Schuster, Inc. New York N.Y.

Gavage - The administration of liquids through a stomach tube, as in forced feeding. Source: Websters New World Dictionary Of American English - Third College Edition. 1991. Published by Simon & Schuster, Inc. New York N.Y.

Geochemical - Root form is Geochemistry - the branch of chemistry dealing with the chemical composition of the earth's crust and the chemical changes that occur there. Source: Websters New World Dictionary Of American English - Third College Edition. 1991. Published by Simon & Schuster, Inc. New York N.Y.

Geophysical - Root form is Geophysics - the science that deals with the physics of the earth including weather, winds, tides, earthquakes, volcanos, etc., and their effect on the earth. Source: Websters New World Dictionary Of American English - Third College Edition. 1991. Published by Simon & Schuster, Inc. New York N.Y.

Physiology - the branch of biology dealing with the functions and vital processes of living organisms or their parts and organs, the functions and vital processes, collectively (of an organism, or of an organ or a system of organs). Source: Websters New World Dictionary Of American English - Third College Edition. 1991. Published by Simon & Schuster, Inc. New York N.Y.

Physiological - of physiology, characteristic of or promoting normal, or healthy, functioning. Source: Websters New World Dictionary Of American English - Third College Edition. 1991. Published by Simon & Schuster, Inc. New York N.Y.

Pinocytosis - the active engulfing of very small particles or liquids by cells; a form of ENDOCYTOSIS. The particles become surrounded by the cell membrane on all sides, which eventually forms a channel from which vesicles are pinched off and move within the PROTOPLASM before their contents can be transferred into the cell proper. Source: The Harper Collins Dictionary of Biology, by: W.G. Hale and J.P. Margham. 1991. Published by HarperCollins Publishers, New York N.Y.

QAPP - Quality Assurance Project Plan

Trabecular - Root form Trabecula - Supporting bundle of fibers crossing the substance of a structure; septum; small piece or spicule of spongy bone. Source: Essential Human Anatomy and Physiology, Second Edition, by Barbara R. Landau, Scott, Foresman and Company Publishers, 1980.